ReveraGen - Vamorolone (VBP15-004)

A Phase IIb Randomized, Double-blind, Parallel Group, Placebo- and Active-controlled Study With Double-Blind Extension to Assess the Efficacy and Safety of Vamorolone in Ambulant Boys With Duchenne Muscular Dystrophy (DMD)

Summary

This Phase 2b study is designed to evaluate the efficacy, safety, pharmacodynamics and pharmacokinetics of vamorolone in comparison to corticosteroids and placebo treatments over a 24 week period. The study will also evaluate the persistence of the effect of vamorolone over a period of 48 weeks.

The study is designed to compare 2 different doses of Vamorolone to a standard dose of corticosteroids (prednisone at 0.75 mg/kg/day) and to a placebo. Across all sites, this trial aimed to recruit a total of 120 ambulant DMD patients ages 4 to <7 years.

Study Number: NCT03439670

Description by ReveraGen BioPharma, Inc.

This Phase IIb study is a randomized, double-blind, parallel group, placebo and active-controlled study to evaluate the efficacy, safety, PD, and population PK of vamorolone administered orally at daily doses of 2.0 mg/kg and 6.0 mg/kg versus prednisone 0.75 mg/kg/day and placebo over a Treatment Period of 24 weeks, and to evaluate persistence of effect over a Treatment Period of 48 weeks in ambulant boys ages 4 to <7 years with DMD.

The study is comprised of a 5-week Pretreatment Screening Period, a 1-day Pretreatment Baseline Period, a 24-week Treatment Period #1 (Weeks 1-24), a 4-week Transition Period (Weeks 25-28), a 20-week Treatment Period #2 (Weeks 28 + 1 day to 48), and a 4-week Dose-tapering Period (Weeks 49-52).

Subjects will be randomized to one of six treatment groups in a 2:2:1:1:1:1 ratio, where the two prednisone groups in Treatment Period #1 (Groups 3 and 4) will be combined and the two placebo groups in Treatment Period #1 (Groups 5 and 6) will be combined, effectively resulting in a 1:1:1:1 randomization (vamorolone 2.0 mg/kg/day : vamorolone 6.0 mg/kg/day : prednisone 0.75 mg/kg/day : placebo) for Treatment Period #1.

Subjects will be stratified based on age at study entry (<6 vs. ≥ 6 years). During the 4-week Transition Period between Treatment Period #1 and Treatment Period #2, all subjects will continue on the same oral suspension (vamorolone 2.0 mg/kg or 6.0 mg/kg, or matching placebo) they received during Treatment Period #1 and all subjects will have their tablet dose tapered to zero. Thus, subjects randomized to receive vamorolone during Treatment Period #1 (Groups 1 and 2) will continue to receive vamorolone at the same dose, while subjects randomized to receive prednisone will have their dose tapered to zero, and subjects randomized to placebo will continue to receive placebo.

The prednisone group will be used as an active control comparison for safety and efficacy endpoints as requested by the European Medicines Agency (EMA). The placebo group will be used as comparator for efficacy endpoints (superiority model) as requested by the EMA and Food and Drug Administration (FDA) protocol advisory board. Although glucocorticoids are part of the care recommendations for DMD, their adverse effect profile has limited their use. The age at which glucocorticoids should be started in DMD boys is uncertain, ranging from 4 to 7 years, based on a balance between benefits and side effects. In view of the age inclusion criteria and duration of the placebo-controlled study period (6 months), the use of a placebo group has been considered acceptable as in clinical practice it will not cause a real delay in prescription of an accepted treatment for this condition. Any exposure of placebo longer than 6 months was considered unethical.

At the end of the Treatment Period #2, subjects may be given access to vamorolone through an additional study or general access program, or given the option to transition to standard of care treatment for DMD (may include glucocorticoids). Subjects completing VBP15-004 and enrolling directly into an additional vamorolone study or general access program to receive vamorolone will not need to taper their vamorolone dose prior to enrollment. All other subjects will begin a 4-week double-blind Dose-tapering Period during which the dose of study medication will be progressively reduced and discontinued.

Primary Outcome Measures

- Efficacy measured by Time to Stand Test (TTSTAND) [Time Frame: 24 weeks]

  vamorolone at 6.0mg/kg/day vs. placebo group in change from baseline to the Week 24 assessment

Secondary Outcome Measures

- Efficacy measured by Time to Stand Test (TTSTAND) [Time Frame: 24 weeks]

  vamorolone at 2.0mg/kg/day vs. placebo group in change from baseline to the Week 24 assessment
- Efficacy as measured by Time to Run/Walk Test (TTRW). [Time Frame: 24 weeks]

  vamorolone at 6.0mg/kg/day vs. placebo group in change from baseline to the Week 24 assessment
- Efficacy as measured by Time to Run/Walk Test (TTRW). [Time Frame: 24 weeks]

  vamorolone at 2.0mg/kg/day vs. placebo group in change from baseline to the Week 24 assessment
- Efficacy as measured by total distance traveled in meters, in completing the Six-minute Walk Test (6MWT) [Time Frame: 24 weeks]

  vamorolone at 6.0mg/kg/day vs. placebo group in change from baseline to the Week 24 assessment

AUSNMD

Trial Status
Trial complete

Locations
Melbourne - Melbourne Children's Campus, Trial complete/terminated, Sydney - Westmead Children's Hospital, Trial complete/terminated

Trial Sponsor
ReveraGen BioPharma, Inc.

Age
4 to under 7 years

Mutation Specific
No

Muscle Biopsy
No

MRI
No

Phase
2b

Length Of Participation
52 weeks

Recruitment Target
120

Ambulatory
Yes

Therapeutic Category
Steroid alternative

- Efficacy as measured by total distance traveled in meters, in completing the Six-minute Walk Test (6MWT) [Time Frame: 24 weeks]

  vamorolone at 2.0mg/kg/day vs. placebo group in change from baseline to the Week 24 assessment

- Efficacy as measured by total distance traveled in meters, in completing the Six-minute Walk Test (6MWT) [Time Frame: 24 weeks]

  vamorolone at 6.0mg/kg/day vs. prednisone group in change from baseline to the Week 24 assessment

- Efficacy as measured by total distance traveled in meters, in completing the Six-minute Walk Test (6MWT) [Time Frame: 24 weeks]

  vamorolone at 2.0mg/kg/day vs. prednisone group in change from baseline to the Week 24 assessment

- Efficacy measured by Time to Stand Test (TTSTAND) [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

- Efficacy as measured by Time to Run/Walk Test (TTRW). [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

- Efficacy as measured by total distance traveled in meters, in completing the Six-minute Walk Test (6MWT) [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

- Efficacy measured by Time to Climb Test (TTCLIMB) [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

- Efficacy as measured by the North Star Ambulatory Assessment (NSAA) [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

- Efficacy as measured by hand-held myometry (elbow flexors and knee extensors) [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

- Efficacy as measured by range of motion in the ankles (ROM) [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment group up to 48 weeks

Other Outcome Measures

- Safety as measured by BMI z-score [Time Frame: 48 weeks]

  Change from baseline to each of the assessment timepoints for each treatment

- Safety as measured by Treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) by system organ class (SOC) [Time Frame: 48 weeks]

  Overall by treatment, by treatment and relationship, and by treatment and intensity

Can I take part?

Inclusion Criteria

- Have a medically confirmed diagnosis of Duchenne Muscular Dystrophy (DMD)
- Be between greater than or equal to (≥) 4 years and less than (<) 7 years of age at the time of enrolment in the study
- Weigh greater than (>) 13.0 kg and less than or equal to (≤) 39.9 kg at the Screening Visit
- Able to walk independently without assistive devices

- Able to complete the Time to Stand Test (TTSTAND) without assistance in <10 seconds, as assessed at the Screening Visit
- Clinical laboratory test results are within the normal range at the Screening Visit, or if abnormal, are not clinically significant, in the opinion of the Investigator.
- Have had chicken pox vaccinations, or have immunity to chicken pox, as determined by:
    - Presence of IgG antibodies to varicella, as documented by a positive test result from the local laboratory from blood collected during the Screening Period, OR
    - Documentation, provided at the Screening Visit, that the subject has had 2 doses of varicella vaccine, with or without serologic evidence of immunity; the second of the 2 immunizations must have been given at least 14 days prior to randomization.
- Be able to swallow tablets
- Subject and parent(s)/guardian(s) are willing and able to comply with scheduled visits, study drug administration plan, and study procedures

Exclusion Criteria

- Subject has current or history of major renal or hepatic impairment, diabetes mellitus or immunosuppression
- Subject has current or history of chronic systemic fungal or viral infections;
- Subject has had an acute illness within 4 weeks prior to the first dose of study medication;
- Subject has used mineralocorticoid receptor agents, such as spironolactone, eplerenone, canrenone (canrenoate potassium), prorenone (prorenoate potassium), mexrenone (mexrenoate potassium) within 4 weeks prior to the first dose of study medication;
- Subject has a history of primary hyperaldosteronism;
- Subject has evidence of symptomatic cardiomyopathy [Note: Asymptomatic cardiac abnormality on investigation would not be exclusionary];
- Subject is currently being treated or has received previous treatment with oral glucocorticoids or other immunosuppressive agents [Notes: Past transient use of oral glucocorticoids or other oral immunosuppressive agents for no longer than 1 month cumulative, with last use at least 3 months prior to first dose of study medication, will be considered for eligibility on a case-by-case basis, unless discontinued for intolerance. Inhaled and/or topical glucocorticoids are permitted if last use is at least 4 weeks prior to first dose of study medication or if administered at stable dose beginning at least 4 weeks prior to first dose of study medication and anticipated to be used at the stable dose regimen for the duration of the study];
- Subject has an allergy or hypersensitivity to the study medication or to any of its constituents;
- Subject has used idebenone within 4 weeks prior to the first dose of study medication;
- Subject has severe behavioral or cognitive problems that preclude participation in the study, in the opinion of the Investigator;
- Subject has previous or ongoing medical condition, medical history, physical findings or laboratory abnormalities that could affect safety, make it unlikely that treatment and follow-up will be correctly completed or impair the assessment of study results, in the opinion of the Investigator;
- Subject is taking (or has taken within 4 weeks prior to the first dose of study medication) herbal remedies and supplements which can impact muscle strength and function (e.g., Co-enzyme Q10, creatine, etc);
- Subject is taking (or has taken within 3 months prior to the first dose of study medication) any medication indicated for DMD, including Exondys51 and Translarna;
- Subject has been administered a live attenuated vaccine within 14 days prior to the first dose of study medication;
- Subject is currently taking any other investigational drug or has taken any other investigational drug within 3 months prior to the first dose of study medication;
- Subject has a sibling who is currently enrolled in any vamorolone study or Expanded Access Program, or who intends to enroll in any vamorolone study or Expanded Access Program during the subject's participation in the VBP15-004 study; or
- Subject has previously been enrolled in the study. Note: Any parameter/test may be repeated at the Investigator's discretion during Screening to determine reproducibility. In addition, subjects may be rescreened if ineligible due to a transient condition which would prevent the subject from participating, such as an upper respiratory tract infection or injury, or if ineligible due to negative anti-varicella IgG antibody test result.

Other inclusion/exclusion criteria apply.

For contact details and to find out more, please refer to ausnmd.org.